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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/830,147	06/11/2001	Kenneth Kellar	NIDN-10	9771
22840	7590	04/08/2004	EXAMINER	
AMERSHAM BIOSCIENCES PATENT DEPARTMENT 800 CENTENNIAL AVENUE PISCATAWAY, NJ 08855			HARTLEY, MICHAEL G	
			ART UNIT	PAPER NUMBER
			1616	

DATE MAILED: 04/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/830,147	KELLAR, KENNETH	
	Examiner	Art Unit	
	Michael G. Hartley	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 November 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 13, 14, 23 and 25-34 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 13, 14, 23 and 25-34 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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Response to Amendment

It is noted that no actual amendment was filed in the response filed 11/17/2003. Applicant states that claim 33 has been canceled in the "remarks/arguments" only. However, this is not a proper amendment for the cancellation of claims, which must include a clean copy of all the pending claims. Thus, the amendment to cancel claim 33 has not been entered.

Response to Arguments

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 33 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for the reason set forth in the office action mailed 8/4/2003.

Applicant's arguments filed 11/17/2003 have been fully considered but they are not persuasive.

Applicant asserts that this rejection has been obviated by the cancellation of claim 33.

This is not found persuasive because claim 33 has not been properly canceled as stated above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 13, 14, 23, 25-29, 33 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Unger (US 5,368,840) in view of either one of Lauffer (US 5,250,285); or Hemmi (US 5,886,173) or Chiu (US 5,344,639), for the reason set forth in the office action mailed 8/4/2003.

Applicant's arguments filed 11/17/2003 have been fully considered but they are not persuasive.

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Applicant asserts that Lauffer teaches chelates which are hydroxy-aryl substituted chelates wherein the aryl groups increase the lipophilicity and are necessary for his compounds to work as blood pool imaging agents while none of the chelates claimed contain hydroxyl aryl groups. Thus, there is not the requisite motivation to pick Eu(II) independent of hydroxy-aryl containing chelates with the chelates of Unger.

This is not found persuasive because Unger teaches the methods and chelates as claimed by specifically reciting a very limited list of chelates, naming specifically EDTA, DOTA and DO3A, as claimed. Unger also teaches that various metals may be used in an equivalent manner, including Eu(III) while for MRI, while Lauffer (as well as, Hemmi and Chui) teaches that Eu(II) is a well known equivalent metal to other paramagnetic metals for MRI. The combination is not relied upon to teach or suggest the chelates of Lauffer, only that Eu(II) is known to be an equivalent MRI metal. One of ordinary skill in the art would have been motivated to employ any paramagnetic MRI metal, as taught by Unger in the chelates disclosed therein, such as Eu(II), as taught by Lauffer. Lauffer teaches that Eu(II) is a metal useful for MRI, not that Eu(II) can only be used with hydroxyl-aryl containing chelates. The art as a whole clearly teaches that Eu(II) is known to be a useful metal in chelates used for MRI imaging, as shown by, Lauffer, Hemmi and Chui.

Applicant asserts that Lauffer teaches that DOTA lacks hydrophobic substituents and thus is unsuitable for NMR of liver and blood pool. Thus, the combination teaches away from Eu(II) DOTA complexes.

This is not found persuasive because Unger teaches that use of DOTA for imaging regions of decreased vascular perfusion, (note, which does not require that the agent is a blood pool agent). Lauffer does teach useful chelates, but is not being relied upon to teach the use of such chelates. Lauffer is only being relied upon to teach that Eu(II) is a well known metal which may be used interchangeably with the same metals disclosed by Unger to provide a paramagnetic metal to the chelate, thus, enhancing MRI.

Applicant asserts that Hemmi does not show the general use of Eu(II) in MRI chelates.

This is not found persuasive because Hemmi clearly teaches the equivalence of Eu(II) to Eu(III), as disclosed by Unger, as an MRI metal, as Hemmi teaches Eu(II) directly next to Eu(III), as set forth in

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column 6, lines 35-50. Also, applicant's cited recitation of the metal being useful for PDT is not seen, as Hemmi states that this is not to be a limiting generalization.

Applicant states that Hemmi only teaches the use of Eu(II) with porphyrins and not with the chelates of Unger and that this would only be "obvious to try."

This is not found persuasive because it is clear from the art as a whole that various metals may be used interchangeably in various chelates for MRI and that the use of Eu(II) is clearly known as a possible metal that may be used as an equivalent to the metals disclosed by Unger.

Applicant asserts that Hemmi is silent to imaging regions of decreased vascular perfusion.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Unger is used to disclose all of the limitations, such as, imaging regions of decreased vascular perfusion, while the secondary references are used to show that Eu(II) is known to be useful as a metal to enhance MRI in chelating agent contrast agents.

Applicant asserts that the combination of references suggests so many combinations that to arrive at the claimed combination would be impermissible, as to the use of the application itself.

This is not found persuasive because Unger clearly discloses that the claimed chelates, DOTA, EDTA and DO3A are specifically preferred chelates for methods of MRI as claimed. The art as a whole clearly shows that Eu(II) is known to be a useful metal for such MRI chelates. Thus, one of ordinary skill in the art would have been motivated to use known MRI metals, such as, Eu(II) which is known in the art, since Unger teaches that any useful MRI metal may be employed.

Applicant asserts that Chui does not teach that Eu(II) is more preferred than any of the other 10 metal ions.

This is not found persuasive because Chui, as does Unger, teaches that any paramagnetic metal may be employed, and specifically teaches that Eu(II) is a preferred metal. Thus, Chui does specifically point to Eu(II) in a very limited number of metals (10) that are especially preferred. Chui also teaches that

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Eu(II) is an equivalent to the metals specifically preferred by Unger. Chui clearly provides a showing of the art as a whole that Eu(II) is a useful metal in MRI chelates.

In sum, Unger teaches the claimed methods, using well known chelates, DOTA, DO3A, DOTA, etc., which are specifically recited in Unger in methods of imaging regions having decreased vascular perfusion and teaches that any paramagnetic metal may be used therein. The art of MRI agents as a whole clearly shows that the use of Eu(II) is equivalent to the metals disclosed by Unger, such as, Eu(III), Gd(III), etc., as disclosed by Unger, and/or that this metal is one that is preferred as an MRI chelate enhancing metal, as shown by, Lauffer, Hemmi and Chui.

Claims 30-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Unger (US 5,368,840) in view of either one of Lauffer (US 5,250,285); or Hemmi (US 5,886,173) or Chiu (US 5,344,639) as applied to claims 13, 14, 23, 25-29, 33 and 34 above, and further in view of Rocklage (US 5,190,744), for the reason set forth in the office action mailed 8/4/2003.

Applicant's arguments filed 11/17/2003 have been fully considered but they are not persuasive.

Applicant asserts that these claims should be allowed on the basis of allowability of their base claims for the reasons set forth above.

As set forth above the base claims are not allowable at this time.

Conclusion

No claims are allowed at this time.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. US 6,652,835 is cited for showing the state of the art in methods of MRI using Eu(II), as well as other equivalent metals, with known chelates, such as, DOTA, etc., for example in claim 1.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

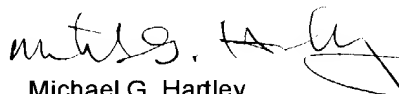
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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael G. Hartley whose telephone number is (571) 272-0616. The examiner can normally be reached on M-F, 7:30-5, off alternative Mondays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Michael G. Hartley
Primary Examiner
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4/5/2004